

# **The Bio-Superior HEPylation™ Drug Delivery System**



**BIO2009 Business Forum**

**May 19, 2009**

Background on the System  
Market Needs/ Issues drug developers  
are facing  
Description of HEPylation™ System  
Technology  
Proof of Concept Studies Highlights  
Technology Differentiation  
Benefits to drug developers  
Variety of partnering opportunities

The HEPylation™ drug delivery system uses a patented composition designed to improve the performance of many powerful drug compounds in terms of

**Safety**

**Tolerability**

**Efficacy**

**Quality**

15 months ago our Chief Scientist, Dr. Paul DeAngelis, conceived the System

Pitched it at BIO2008 to confirm the market's desire for it and what data the drug developers needed

Designed and implemented the Proof of Concept studies and obtained the necessary data

Filed patent applications

## **Most powerful drugs are**

- Difficult to administer
- Painful
- Highly reactive with the immune system

Making them unsuitable for use in native form

## **The PEG molecule addresses these problems BUT it has inherent limitations / functional issues**

- Toxicity
- Accumulation in the liver and brain
- Potential immunogenicity
- Problematic syntheses
- Patents which are tightly controlled
- Restrictive/expensive licensing rights

**The HEPylation™ Drug Delivery System** is the process of conjugating a naturally occurring sugar molecule, heparosan, to a drug.

It has many advantages over PEG and other delivery systems.

## It is “bio-inert”.

The body produces no extracellular enzymes that degrade it, and there are no known receptors or binding proteins for heparosan.

## It is “bio-stealthy”.

The immune system does not see it, so it does not make antibodies against it (in fact certain pathogens employ this polymer as molecular camouflage!).

It is “**bio-compatible**”.

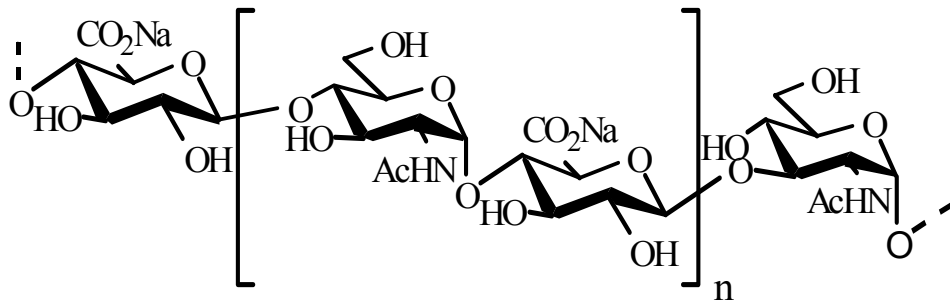
It is made in the body thus causing no harm when eventually degraded.

## It is “bio-flexible”

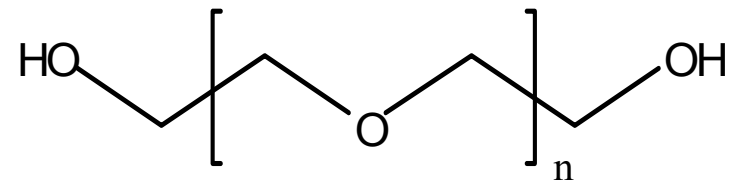
Larger size heparosan polymers can be made in a uniform, “monodisperse” manner.

**Unlike PEG, Heparosan possesses many negative groups and is replete with hydroxyl groups.**

**Heparosan**



**Polyethylene glycol**



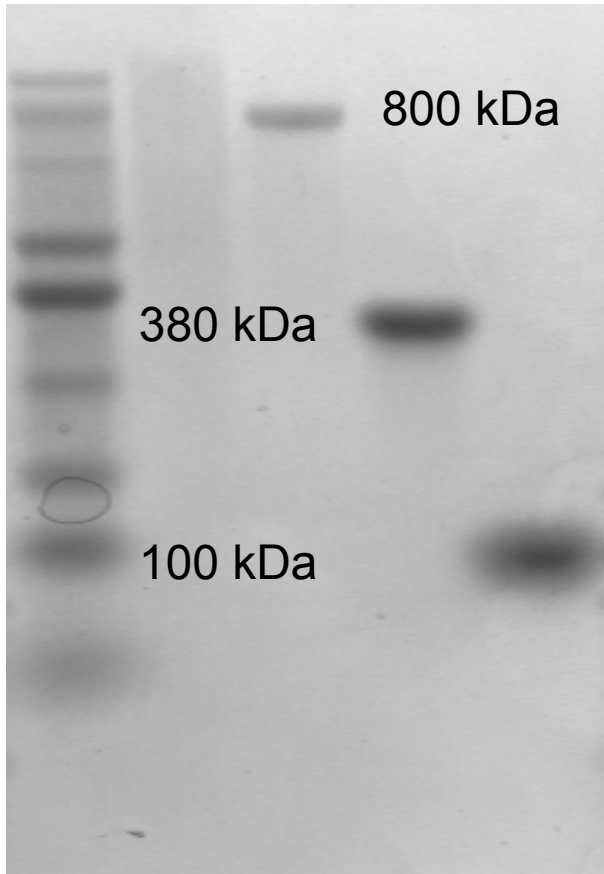
**Heparosan is more soluble than PEG.**

**The HEPylation™ System is bio-superior to PEG.**

- No known toxic effects
- Longer residence (circulation) time of the drug in the body
- Greater uptake of drug
- Safe absorption/excretion
- A range of therapeutic dosing profiles
- Adaptable to many drugs
- New and Novel Intellectual Property

## 3 Pharmacokinetic (PK) studies in small animals with several polymer sizes

- Polymer production reproducibility
  - Monodispersity = 1.06 to 1.18
- Monodisperse polymers of wide size range 10 to 800kDa
- Data indicates > 2x increase in half-life over PEG of similar size
- Stable in bloodstream
- No detectable accumulation in organs
- Degrades into simple sugars that are recycled or excreted
- Easy cargo conjugation/multiple types of linkage
- IM/IP study with 100kDa heparosan
  - Yielded >50% increase v. intravenous injection (IV)
- Rheology study confirmed heparosan is not viscous – thus “injection” friendly

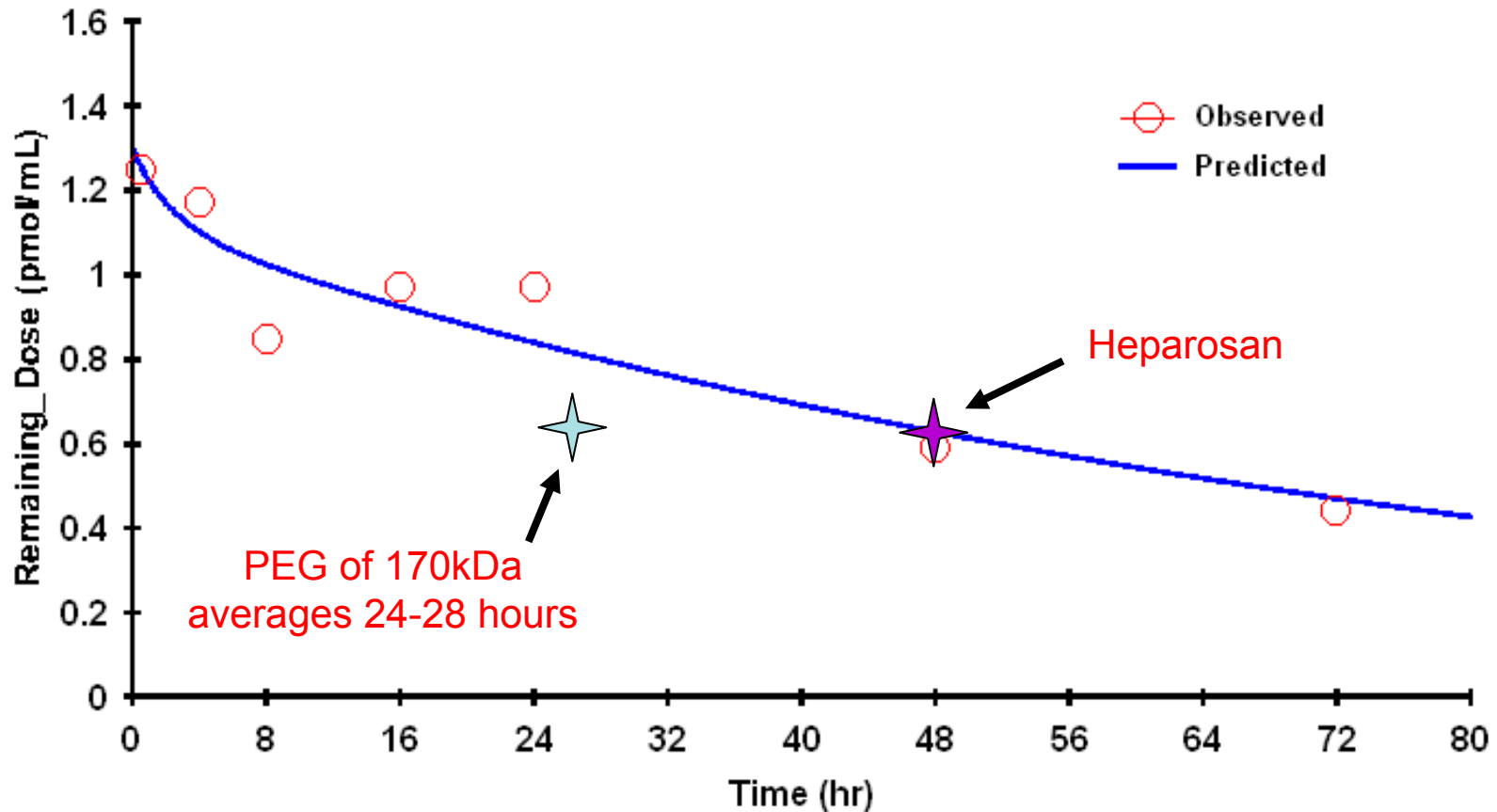


This is not a one size fits all molecule! These are representative of the production flexibility.

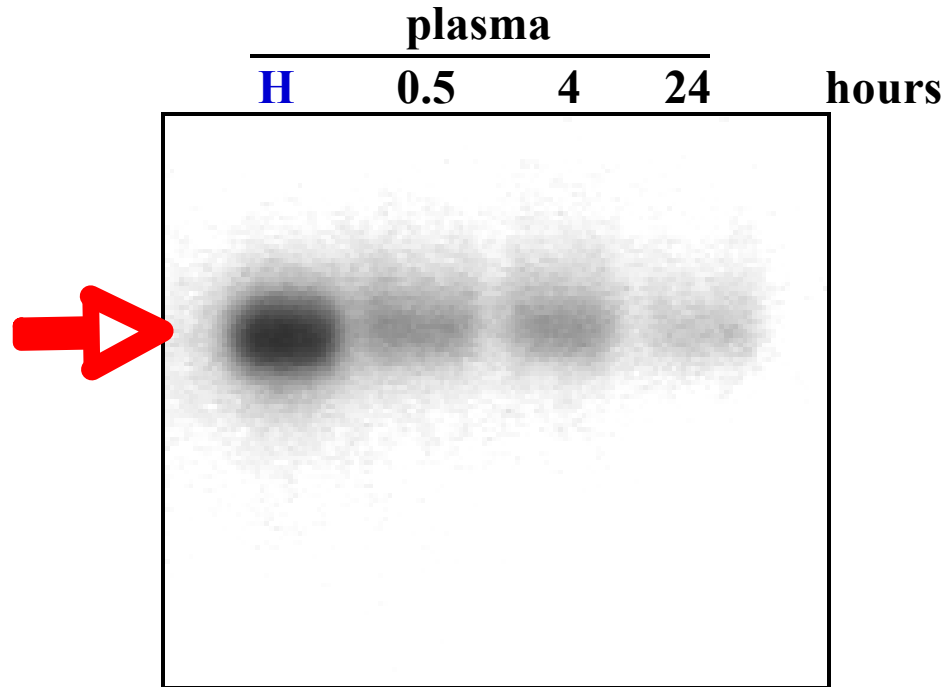
The HEPylation™ system allows tuning of **therapeutic dosing profiles**.

## Synthesis of Monodisperse Heparosan Polymers

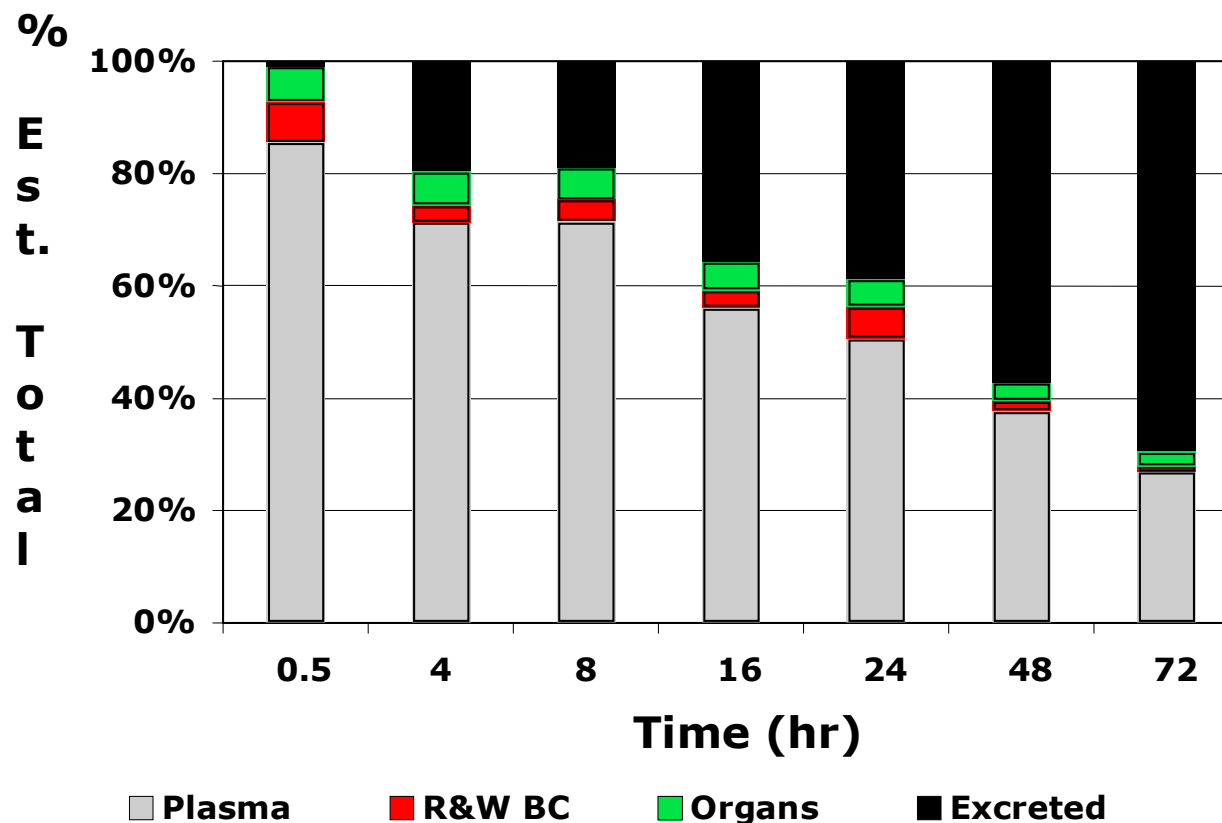
# Technology – Half-life study



**Pharmacokinetics of Radioactive Heparosan in Plasma in a Rat Model: Long Lifetime (~2 day half-life)**

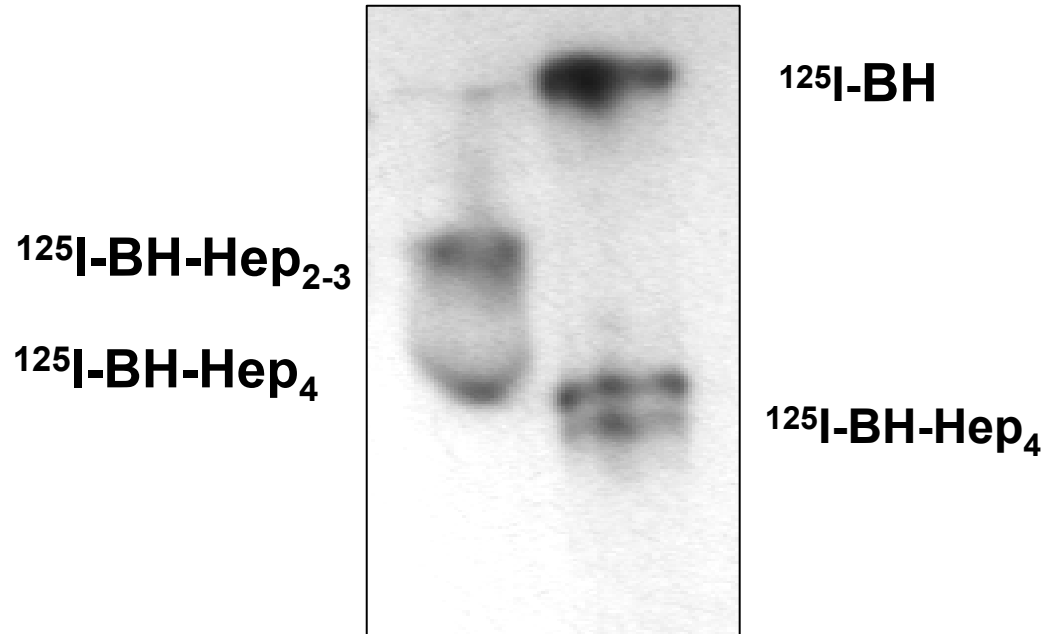


**Heparosan is very stable in the mammalian bloodstream.**



**Fate of Radioactive Heparosan in a Rat Model:  
Did not accumulate in major organs.**

## Urine Standard



**Probe in feces is also similarly degraded to ~ 2-4 sugars.**

**Caisson Biotech** has exclusive rights to

- 2 issued patents
- 10 pending patents

Domestic and foreign coverage

In compositions and methods

## Grant Received

- Oklahoma Center for Advancement of Science and Technology – Oklahoma Applied Research Support (**OCAST/OARS**)
- December 2008 for \$300,000

## Grant Anticipated to be Received

- National Institute of General Medical Sciences – Small Business Technology Transfer (**STTR Phase 1**)
- May 2009 for \$219,000

**Working towards a GMP Production capability for Heparosan through an Oklahoma EDGE grant**

## **HEPylation™ benefits to drug developers**

- Opens new markets for their drugs
- Facilitates re-tooling of their existing drugs for market life extension
- Improves their drugs' PK performances
- New patent protection

**Providing a paradigm shift in patient care and better compliance in multiple therapeutic areas**

The HEPylation™ bio-superior drug delivery system is suitable for

- Joint development with drug developers with their own drug candidates
- Drug developers wanting to license our HEPylated™ drug candidates
- Drug developers wanting the supply of Heparosan and the rights to use the HEPylation™ system for their own drug conjugate development program.

# Acknowledgements

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**Dr. Paul DeAngelis, Chief Scientist**

**William Strieber, Executive Vice President**

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**Nicole Menteer, Manager - Marketing and  
Communications**

**and the Emergent Technologies, Inc. team**

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